Remarks

Claims 1, 5, 6, 7 and 8 are amended. Claims 1-10 and 12-17 are pending in this application. Claim 1 is directed to a method of stimulating an HIV-specific $CD8^+$ T response. Support for this subject matter can be found throughout the specification as originally filed, for example, in the Summary of the Invention, at page 14, line 22 to page 15, line 9 and in the Examples. Claim 1 further defines the types of HIV specific peptides contemplated, including HIV gag, gp120, nef or pol peptides. Support for this subject matter can be found throughout the specification as originally filed, for example, at page 11, lines 6-20. Claims 5-8 depend ultimately from claim 1 and are drawn to different types of recombinant viral vectors. Support for this subject matter can be found throughout the specification, for example, at page 6, line 4 to page 9, line 13 and the Examples. Applicant submits that these amendments add no new matter.

Personal Interview

Applicant wishes to thank the Examiner for extending the courtesy of a personal interview to Applicant's representative, Robin A. Chadwick, on March 29, 2005.

The issues raised in the Office Action were discussed. The Examiner suggested that "HIV-specific" CD8+ response would be acceptable in claim 1 in place of an "efficient" CD8+ response. Applicant's representative offered to file a Declaration by Dr. Franchini to further illustrate the invention. The Examiner indicated that he would consider claims drawn to administering recombinant poxvirus vaccines encoding specific types of HIV peptides/antigens so long as support existed in the application for these embodiments.

This account is believed to be a complete and accurate summary of the interview as required by 37 C.F.R. § 1.133. If the Examiner believes that this summary is inaccurate or incomplete, Applicants respectfully request that the Examiner point out any deficiencies in his

35 U.S.C. § 112, Second Paragraph, Rejection

Claims 1-10 and 12-17 were rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for allegedly being indefinite for use of the phrase "efficient CD8+ response." The Examiner also alleges that reference to administration of a recombinant virus in claims 5-8 is indefinite because a nucleic acid-based vaccine is being administered.

Claim 1 is currently directed to a method of stimulating an HIV-specific $CD8^+$ T-cell response by administering a recombinant viral vaccine. During the March 29, 2005 telephone interview, the Examiner suggested that "HIV-specific" would be acceptable. Applicant has amended claim 1 as suggested by the Examiner. Applicant has further clarified the language of claims 1, 5-8 with regard to the recombinant viral vaccine now administered as described in claim 1.

Applicant submits that the language of the claims is definite and in conformance with 35 USC 112, second paragraph. Withdrawal of the 35 U.S.C. 112, second paragraph, rejection is respectfully requested.

35 U.S.C. § 112, First Paragraph, Rejection

Claims 1-10 and 12-17 were rejected under 35 U.S.C. § 112, first paragraph, as allegedly lacking enablement. The Examiner has alleged the invention lacks working examples and a teaching about how one can overcome the alleged well known difficulties in the field of HIV-1 vaccine development.

The test for enablement is whether one reasonably skilled in the art could make or use the invention from the disclosures in the patent coupled with information known in the art without undue experimentation. *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 231 U.S.P.Q. 81, 94 (Fed. Cir. 1986), cert. denied, 480 U.S. 947 (1987).

Applicants need not describe every nuance of the invention in order to satisfy the requirements of 35 U.S.C. § 112. In particular, that which is known need not be described in the application. For example, sequences for HIV peptides and nucleic acids, for example, Gag, Pol, Pro, Tat, Nef, Rev, Vif, Vpr and Env peptides and nucleic acids are publicly available and need not be listed in the application. At the time of filing, one of skill in the art could readily insert nucleic acids encoding such peptides into recombinant pox viruses or generate a DNA vaccine using the procedures described in the application. Hence, the specification clearly enables one of skill in the art to make and use the invention.

Claim 1 is directed to a method of stimulating an HIV1-specific $CD8^+$ response in a human infected with a HIV retrovirus said method comprising: administering to the human, a recombinant viral vaccine, which enters the cells of the human and intracellularly produces HIV-

specific peptides for presentation on the cell's MHC class I molecules, where said peptides are presented in an amount sufficient to stimulate a protective $CD8^+$ HIV structural antigen response, and where said human (i) has a viral load of less than 10,000 viral copies per ml of plasma and a $CD4^+$ cell count of above 500 cells/ml, and (ii) has been treated with one or more anti-viral agents, which contributed to a lower viral copy and higher $CD4^+$ cell count than before treatment; where said HIV specific peptides comprise HIV gag, gp120, nef or pol peptides.

Applicant submits that the specification fully enables the claimed invention because, since the filing date of the present invention, researchers have shown that administration of recombinant viral vaccines that encode HIV1-specific peptides do stimulate an HIV1-specific $CD8^+$ response. Applicant provides herewith a Declaration under 37 C.F.R. §1.132 and an Information Disclosure Statement with articles illustrating the efficacy of various recombinant viral vaccines that encode HIV1 peptides.

The Declaration by Dr. Genoveffa Franchini describes two clinical trials conducted by Aventis Pasteur as well as proposed clinical trials by EuroVacc. The clinical trials involved administration of a recombinant pox virus that encoded HIV peptides (vCP1452) to human HIV-infected patients. In the ACTG5054 Trial, the patients had been undergoing antiretroviral therapy (ART) and prior to administration of vCP1452 had a median CD4 count of 609 and a viral load of less than 50 (see pages 3 and 5 of the Declaration Appendix). Preliminary results indicate that patients who received the recombinant vCP1452 pox virus alone had a lower viral load than those who received placebo (page 5 of the Declaration Appendix)). In the Quest trial, patients who received the recombinant pox virus had increased CD4 and CD8 responses at week 24 (see page 11 of the Declaration Appendix).

A press release by EuroVacc, which is provided with the Supplemental Information Disclosure Statement filed herewith, describes results from a NYVAC-HIV C vaccine trial. *See* article entitled, "Results from EV01 HIV Vaccine Trial, London and Lausanne, July 7th, 2004." The vaccine employed a highly attenuated recombinant vaccinia virus that expresses *gag*, *pol*, *nef* and *env* synthetic genes of HIV-1 clade C. *Id.* As reported, the vaccine was well-tolerated by the 24 people who received it. *Id.* Vaccine-induced anti-HIV T-cell responses were observed in 5/12 (45%) of the vaccine recipients using stringent quality controlled clinical lab assays. *Id.* *Env*-specific responses were found in all 5 responding subjects but additional responses against

other proteins of HIV (e.g. Gag and Nef) were detected in 40% of the responders. *Id.* Anti-env antibodies, analyzed at the University of Oxford, were detected in 5/24 (20%) of volunteers at week 4. *Id.* Hence, administration of recombinant pox viruses has beneficial effects.

Moreover, several additional articles listed and provided with the Supplemental Information Disclosure Statement (filed herewith) illustrate the efficacy of various HIV vaccines.

For example, the article by Jin et al. (J. Virol. 76: 2206-16 (2002)) shows that administration of the ALVAC vCP1452 recombinant virus stimulates an HIV1-specific $CD8^+$ response in HIV-infected patients who have been receiving antiretroviral therapy. Patients included in this study were infected with HIV but had a viral load of 50 copies HIV-1 RNA per ml plasma and an average CD4 count of 779 (see page 2207). As stated at page 2211 of the Jin et al. article, 78% of patients had an increase in $CD8^+$ T-cell responses to at least one HIV-1 antigen (see also Figure 4b and pages 2213-14). The recombinant vCP1452 virus is a recombinant pox virus that encoded gp120, gp41, p55, pol and nef HIV peptides (*id.* at page 2207).

In another study, macques vaccinated with an HIV-1 clade B vaccine (expressing gag, pol and env proteins) elicit CD8+ T cell responses that recognize another HIV-1 clade (A/G) better than the CD4 T cells of those macques. *See* Smith et al. AIDS Res. Human Retrovir. 21: 140-144 (2005). Hence, HIV1 peptides from a variety of HIV-1 strains or clades can stimulate an HIV1-specific CD8+ response even when the animal or patient becomes exposed to a new variety, strain or clade of HIV-1.

Thus, Applicant submits that the claimed invention is fully enabled by the specification and respectfully requests withdrawal of this rejection under 35 U.S.C. §112, first paragraph.

Conclusion

Applicant respectfully submits that the claims are in condition for allowance, and notification to that effect is earnestly requested. The Examiner is invited to telephone Applicant's attorney at (516) 795-6820 to facilitate prosecution of this application.

If necessary, please charge any additional fees or credit overpayment to Deposit Account No. 19-0743.

Respectfully submitted,

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Date May 16, 2005

By _____
Robin A. Chadwick
Reg. No. 36,477

CERTIFICATE UNDER 37 CFR 1.8: The undersigned hereby certifies that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail, in an envelope addressed to: Commissioner of Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on this 16TH day of May, 2005.

PATRICIA A. HULTMAN

Name

Signature